Clinical trial results:
Colon staining efficacy of single oral doses of methylene blue MMX® modified release tablets administered to patients undergoing colonoscopy

Summary

EudraCT number	2011-001173-24
Trial protocol	IT
Global end of trial date	24 September 2012

Results information

Result version number	v1 (current)
This version publication date	29 December 2022
First version publication date	29 December 2022

Trial information

Trial identification

Sponsor protocol code	CB-17-01/03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cosmo Technologies Ltd
Sponsor organisation address	Riverside II, Dublin, Ireland, D02 KV60
Public contact	sduggan@cosmopharma.com, Sarah Duggan, 353 018170370, llongo@cosmopharma.com
Scientific contact	llongo@cosmopharma.com, Luigi Longo, 353 018170370, llongo@cosmopharma.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 January 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 January 2012
Global end of trial reached?	Yes
Global end of trial date	24 September 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe and evaluate the mucosal staining efficacy of methylene blue MMX 25mg modified tablets after single oral doses of 150 or 200mg in patients undergoing a full colonoscopy for various reasons.

Protection of trial subjects:

Before being admitted to the clinical study, subjects expressed their consent to participate and to the access to their confidential data. The investigator explained the nature, scope and possible consequences of the clinical study in an understandable form. Information was provided to the subjects in both oral and written form. On the day after (day 2), the patients returned to the clinic for colonoscopy. The investigator inquired the subjects about occurrence of any AE and the intake of concomitant medications. Vital signs (BP, HR, SpO2) were measured prior to, during and after the end of the colonoscopy.

Background therapy:

NA

Evidence for comparator:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3.

Actual start date of recruitment	02 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 122
Worldwide total number of subjects	122
EEA total number of subjects	122

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	92
From 65 to 84 years	30
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3.

Pre-assignment

Screening details:

All subjects received a full dose regimen of a 4-L PEG-based bowel cleansing preparation available on the market, following the instructions enclosed with the product, starting in the afternoon before the colonoscopy day

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

NA

Arms

Are arms mutually exclusive?	Yes
Arm title	MB-MMX-150mg

Arm description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

Arm type	Experimental
Investigational medicinal product name	Methylene Blue MMX® modified release tablets
Investigational medicinal product code	CB-01-17
Other name	LumeBlue
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pharmaceutical form
modified release tablets
Strength
25 mg
Administration route
oral
Batch N.
6324/3 and 6324/4
Expiry date
FEB12

Arm title	MB-MMX-200mg

Arm description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject

number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

Arm type	Experimental
Investigational medicinal product name	Methylene Blue MMX® modified release tablets
Investigational medicinal product code	CB-01-17
Other name	LumeBlue
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pharmaceutical form
modified release tablets
Strength
25 mg
Administration route
oral
Batch N.
6324/3 and 6324/4
Expiry date
FEB12

Number of subjects in period 1	MB-MMX-150mg	MB-MMX-200mg
Started	25	97
Completed	23	86
Not completed	2	11
Consent withdrawn by subject	1	7
Physician decision	-	2
Adverse event, non-fatal	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	122	122	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	92	92	
From 65-84 years	30	30	
85 years and over	0	0	
Age continuous			
Age			
Units: years			
arithmetic mean	54.7		
standard deviation	± 11.2	-	
Gender categorical Units: Subjects			
Female	54	54	
Male	68	68	

End points

End points reporting groups

Reporting group title	MB-MMX-150mg

Reporting group description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

Reporting group title	MB-MMX-200mg

Reporting group description:

Study subjects had to be assigned to either dose of methylene blue in a ratio of 1:1. Therefore, individual doses of 150 mg of Methylene Blue MMX® tablets were initially packaged up to subject number 063 and individual doses of 200 mg were packaged from number 064 to 126 with product batch 6324/3. After protocol amendment 2, additional 50 individual kits from subject number 127 to 176 were packaged with product batch 6324/4 and supplied to the clinical centre. Irrespective of the inclusion date, individual drug supplies of 150 mg were dispensed up to number 025, whereas individual kit of 200 mg were dispensed up to study termination from number 064 to number 160. In conclusion, 24 subjects received 150 mg of methylene blue, whilst 90 subjects received 200 mg of methylene blue (see § 10.1 for details on subjects' disposition). Individual drug supplies from 026 to 063 and from 161 to 176 remained unused.

Subject analysis set title	Analysis of mucosal staining data with 150mg
Subject analysis set type	Per protocol

Subject analysis set description:

Per Protocol population: all enrolled subjects who fulfilled the study protocol requirements in terms of study drug intake and collection of efficacy data, without major deviations that might affect study results.

Subject analysis set title	Analysis of mucosal staining data with 200mg
Subject analysis set type	Per protocol

Subject analysis set description:

Per Protocol population: all enrolled subjects who fulfilled the study protocol requirements in terms of study drug intake and collection of efficacy data, without major deviations that might affect study results.

Primary: Evaluation of the mucosal staining efficacy with MB-MMX 150mg

End point title	Evaluation of the mucosal staining efficacy with MB-MMX 150mg[1]

End point description:

Frequency of staining quality scores (SC) observed in each colonic region in the PP (N=23) and the FAS population (N=24) after 150 mg of Methylene Blue MMX®

End point type	Primary

End point timeframe:

Day of colonoscopy

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: According to the protocol, the subjects were to be assigned to 150 or 200 mg of methylene blue in a ratio of 1:1. Consecutively treated subjects should have received either dose alternatively. Notwithstanding, subjects' allocation to either dose had a ratio of 1:3.67 in the FAS population. The dose of 150 mg was received by 24 subjects, whereas the dose of 200 mg was received by 88 subjects in the FAS population (see § 10.1 for details on subjects' disposition and § 9.4.3 for details of assignme

End point values	Analysis of mucosal staining data with 150mg			
Subject group type	Subject analysis set			
Number of subjects analysed	23			
Units: 23				
Score 0	28			
Score 1	27			
Score 2	11			
Score 3	11			
Score 4	15			
Score 5	0			

Statistical analyses

No statistical analyses for this end point

Primary: Evaluation of the mucosal staining efficacy with MB-MMX 200mg

End point title	Evaluation of the mucosal staining efficacy with MB-MMX 200mg[2]

End point description:

Frequency of staining quality scores observed in each colonic region in the PP (N=86) and the FAS population (N=88) after 200 mg of Methylene Blue MMX

End point type	Primary

End point timeframe:

Day of colonoscopy

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: According to the protocol, the subjects were to be assigned to 150 or 200 mg of methylene blue in a ratio of 1:1. Consecutively treated subjects should have received either dose alternatively. Notwithstanding, subjects' allocation to either dose had a ratio of 1:3.67 in the FAS population. The dose of 150 mg was received by 24 subjects, whereas the dose of 200 mg was received by 88 subjects in the FAS population (see § 10.1 for details on subjects' disposition and § 9.4.3 for details of assignme

End point values	Analysis of mucosal staining data with 200mg			
Subject group type	Subject analysis set			
Number of subjects analysed	86			
Units: 86				
Score 0	49			
Score 1	50			
Score 2	59			
Score 3	77			
Score 4	106			
Score 5	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Day of the colonoscopy	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	15
Reporting groups	
Reporting group title	Gastrointestinal

Reporting group description: -

Serious adverse events	Gastrointestinal		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 114 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 2.6 %

Non-serious adverse events	Gastrointestinal		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 114 (2.63%)		
Gastrointestinal disorders			
Vomiting	Additional description: vomiting		
subjects affected / exposed	3 / 114 (2.63%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

NA

Notes: